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NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

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FULL ESTIMATED COST	0.21	0.21

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DICTIONARY FILE UPDATES: 17 JUL 2006 HIGHEST RN 893880-40-5

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L1 STRUCTURE UPLOADED

=> s l1 ful
FULL SEARCH INITIATED 07:03:27 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 174 TO ITERATE

100.0% PROCESSED 174 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

L2 2 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION
FULL ESTIMATED COST 167.38 167.59

FILE 'CAPLUS' ENTERED AT 07:03:35 ON 18 JUL 2006
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FILE COVERS 1907 - 18 Jul 2006 VOL 145 ISS 4
FILE LAST UPDATED: 17 Jul 2006 (20060717/ED)

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=> s l2
L3 5 L2

=> d his

(FILE 'HOME' ENTERED AT 07:01:47 ON 18 JUL 2006)

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L1 STRUCTURE UPLOADED
L2 2 S L1 FUL

FILE 'CAPLUS' ENTERED AT 07:03:35 ON 18 JUL 2006
L3 5 S L2

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L1 HAS NO ANSWERS
L1 STR
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

Structure attributes must be viewed using STN Express query preparation.

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L3 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:376050 CAPLUS
DN 141:184918
TI Cinnamic acid based thiazolidinediones inhibit human P450c17 and 3β-hydroxysteroid dehydrogenase and improve insulin sensitivity independent of PPARγ agonist activity
AU Arlt, Weibke; Neogi, Partha; Gross, Coleman; Miller, Walter L.
CS Department of Pediatrics and the Metabolic Research Unit, University of California, San Francisco, CA, 94143-0978, USA
SO Journal of Molecular Endocrinology (2004), 32(2), 425-436
CODEN: JMLEEI; ISSN: 0952-5041
PB Society for Endocrinology
DT Journal
LA English
AB Thiazolidinediones improve insulin sensitivity in type 2 diabetes mellitus by acting as peroxisome proliferator-associated receptor gamma (PPARγ) agonists, and decrease circulating androgen concns. in polycystic ovary syndrome by unknown mechanisms. Some thiazolidinediones directly inhibit the steroidogenic enzymes P450c17 and 3β-hydroxysteroid dehydrogenase type II (3βHSDII) by distinct mechanisms. We synthesized five novel thiazolidinediones, CLX-M1 to -M5 by linking a 2,4-thiazolidinedione moiety to a substituted α-Ph cinnamic acid previously shown to have glucose-lowering effects. Using yeast microsomes expressing human P450c17 and 3βHSDII we found that cinnamic acid Me esters with a double bond in the thiazolidinedione core structure (M3, M5) were stronger inhibitors of P450c17 than Me esters with the conventional core (M1, M4). These four compds. inhibited 3βHSDII equally well, while the free cinnamic acid analog (M2) did not inhibit either enzyme. Thus, the inhibition of P450c17 and 3βHSDII by these novel thiazolidinediones reveals

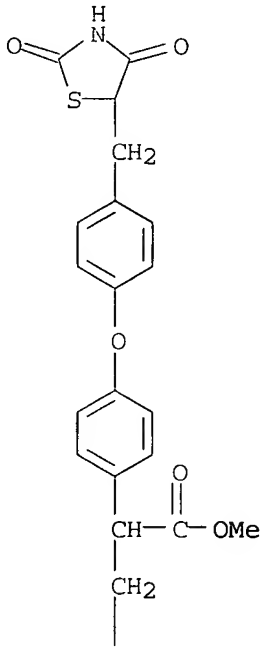
structure-activity relationships independent of PPARγ transactivation. PPARγ transactivation was moderate (M1), weak (M2, M3) or even absent (M4, M5). While the PPARγ agonist activity of M1 was only 3% of that of rosiglitazone, both increased glucose uptake by 3T3-L1 adipocytes and reduced serum glucose levels in ob/ob and db/db mice to a similar extent. The similar glucose-lowering effects of M1 and rosiglitazone, despite their vast differences in PPARγ agonist activity, suggests these two actions may occur by sep. mechanisms.

IT 380881-51-6
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)
(cinnamic acid based thiazolidinediones inhibit human P450c17 and 3β-hydroxysteroid dehydrogenase and improve insulin sensitivity independent of PPARγ agonist activity)

RN 380881-51-6 CAPLUS

CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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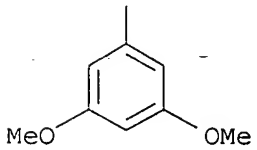

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN

CAS ONLINE PRINTOUT

AN 2003:757334 CAPLUS
DN 139:276885
TI Preparation of novel heterocyclic analogs of diphenylethylene compounds as antidiabetics
IN Neogi, Partha; Dey, Debendranath; Medicherla, Satyanarayana; Nag, Bishwajit; Lee, Arthur
PA USA
SO U.S. Pat. Appl. Publ., 66 pp., Cont.-in-part of U.S. Ser. No. 843,167.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003181494	A1	20030925	US 2002-265902	20021008
	US 2002025975	A1	20020228	US 2001-785554	20010220
	US 2002032225	A1	20020314	US 2001-843167	20010427
	CA 2501456	AA	20040422	CA 2003-2501456	20031008
	WO 2004033438	A1	20040422	WO 2003-US31803	20031008
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	EP 1549625	A1	20050706	EP 2003-774638	20031008
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	CN 1708486	A	20051214	CN 2003-80101164	20031008
	JP 2006505551	T2	20060216	JP 2004-543490	20031008
PRAI	US 1999-287237	A2	19990406		
	US 2000-591105	B2	20000609		
	US 2001-785554	A2	20010220		
	US 2001-843167	A2	20010427		
	US 1998-74925	A2	19980508		
	US 2002-265902	A	20021008		
	WO 2003-US31803	W	20031008		

OS MARPAT 139:276885
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; Z = II-IV; n, m, q and r = 0-4 (n+m ≤ 4 and q+r ≤ 4); p, s = 0-5 (p+s ≤ 5); R, R2 = H, alkyl, alkenyl, etc.; R1 = H, alkyl, alkenyl, etc.; A, A1, A2 = H, acylamino, acyloxy, alkanoyl, etc.; B, B1, B2 = H, acylamino, acyloxy, alkanoyl, etc.; or A and B together, or A1 and B1 together, or A2 and B2 together, may be joined to form a methylenedioxy or ethylenedioxy; X, X1 = (un)substituted NH, O, S] which are effective in lowering blood glucose level, serum insulin, triglyceride and free fatty acid levels in animal models of Type II diabetes, were prepared E.g., a multi-step synthesis of V, starting from 3,5-dimethoxybenzaldehyde and 4-hydroxyphenylacetic acid, was given. The compound V showed strong glucose lowering activity even though it is a weak

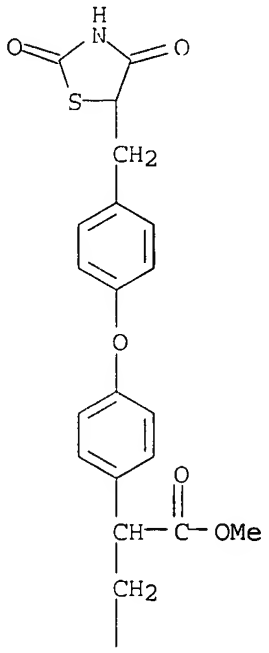
PPAR-γ agonist (data given). The compds. I are disclosed as useful for a variety of treatments including the treatment of inflammation, inflammatory and immunol. diseases, insulin resistance, hyperlipidemia, coronary artery disease, cancer and multiple sclerosis. Pharmaceutical composition comprising the compound I was claimed.

IT 380881-51-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of diphenylethylene compds. containing thiazolidinedione or oxazolidinedione moieties for treating diabetes, inflammatory or immunol. disease in combination with other agents)

RN 380881-51-6 CAPLUS

CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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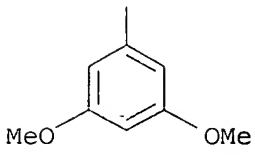

IT 380881-49-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of diphenylethylene compds. containing thiazolidinedione or oxazolidinedione moieties for treating diabetes, inflammatory or

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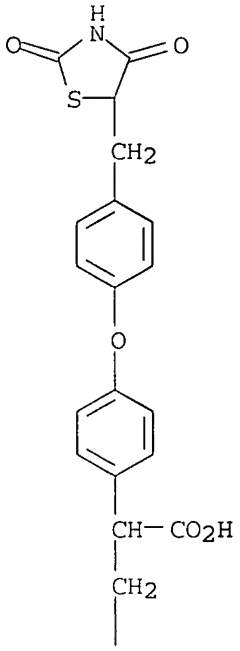
immunol. disease in combination with other agents)
RN 380881-49-2 CAPLUS
CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy- (9CI) (CA INDEX NAME)

PAGE 1-A



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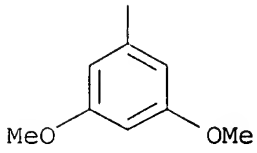

L3 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:645701 CAPLUS
DN 140:87046
TI Synthesis and structure-Activity relationship studies of cinnamic acid-based novel thiazolidinedione antihyperglycemic agents
AU Neogi, Partha; Lakner, Fredrick J.; Medicherla, Satyanarayana; Cheng, Jin; Dey, Debendranath; Gowri, Maya; Nag, Bishwajit; Sharma, Somesh D.; Pickford, Lesley B.; Gross, Coleman
CS Department of Chemistry, Calyx Therapeutics Inc., Hayward, CA, 94545, USA
SO Bioorganic & Medicinal Chemistry (2003), 11(18), 4059-4067
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
OS CASREACT 140:87046
GI

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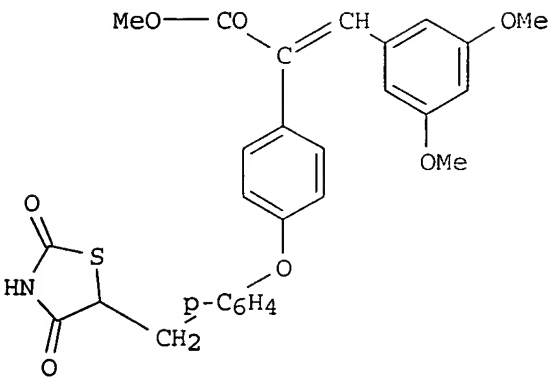


I

AB A number of 2,4-thiazolidinedione derivs. of -Ph substituted cinnamic acid were synthesized and studied for their PPAR agonist activity. The E-isomer of cinnamic acid, I, showed moderate PPAR transactivation. The corresponding Z-isomer and double bond reduced derivative were found to be much less potent. Although the E-isomer showed a moderate PPARγ transactivation, it demonstrated a strong glucose-lowering effect in a genetic rodent model of diabetes. Results of pharmacokinetic, metabolism and permeability studies are consistent with I being an active prodrug with the hydrolyzed carboxylate as an active metabolite that has similar glucose lowering and PPARγ agonist properties.

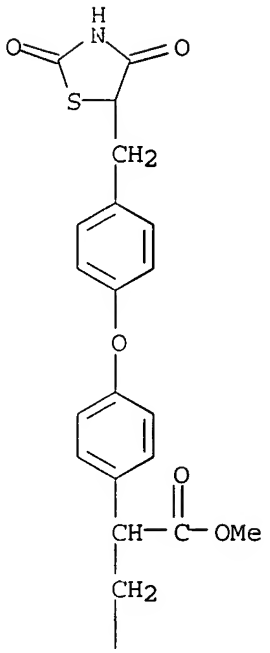
IT 380881-51-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(cinnamic acid-based thiazolidinedione antihyperglycemic agents)

RN 380881-51-6 CAPLUS

CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)

CAS ONLINE PRINTOUT

PAGE 1-A



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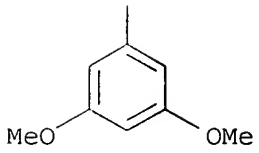

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:185699 CAPLUS
DN 136:247571
TI Preparation of novel heterocyclic analogs of diphenylethylene compounds as inhibitors of cytokines or cyclooxygenase
IN Nag, Bishwajit; Dey, Debendranath; Medicherla, Satyanarayana; Neogi, Partha
PA USA
SO U.S. Pat. Appl. Publ., 34 pp., Cont.-in-part of U.S. Ser. No. 785,554. CODEN: USXXCO
DT Patent
LA English
FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002032225	A1	20020314	US 2001-843167	20010427
	US 6245814	B1	20010612	US 1998-74925	19980508
	US 2002025975	A1	20020228	US 2001-785554	20010220
	CA 2410171	AA	20011220	CA 2001-2410171	20010605
	WO 2001095859	A2	20011220	WO 2001-US17950	20010605
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

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WO	2001-US17950	W	20010605		

OS MARPAT 136:247571

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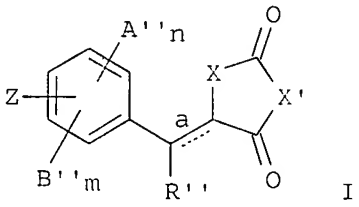

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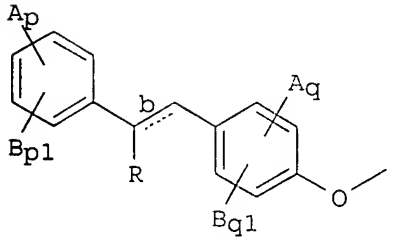

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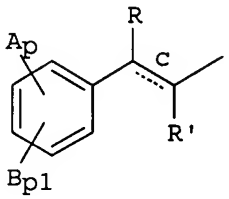


AB Novel diphenylethylene compds. and derivs. thereof containing thiazolidinedione or oxazolidinedione-moieties are provided which are effective in lowering blood glucose level, serum insulin, triglyceride and free fatty acid levels in animal models of Type II diabetes. The above compds. and their derivs. are resented by formula [I; Z = Q, Q1, H, A", B"; wherein n, m, q, q1 = integers from zero to 4 provided that n+m≤4 and q+q1≤4; p, p1 = integers from zero to 5 provided that p+p1≤5; a, b and c are double bonds which may be present or absent; when present; the double bonds may be in the E or Z configuration and, when absent, the resulting stereocenters may have the R- or S-

configuration; R, R', R" = H, C1-20 linear or branched alkyl, C2-20 linear or branched alkenyl, CO2Z' (wherein Z' = H, Na, K, or other pharmaceutically acceptable counterion such as Ca, Mg, ammonium, tromethamine, and the like), CO2R''', NH2, NHR''', N(R''')2, OH, OR''', halo, substituted C1-20 linear or branched alkyl or substituted C2-20 linear or branched alkenyl (wherein R''' is C1-20 linear or branched alkyl or linear or branched alkenyl); A, A', A'' = H, C1-20 acylamino, C1-20 acyloxy, C1-20 alkanoyl, C1-20 alkoxycarbonyl, C1-20 alkoxy, C1-20 alkylamino, C1-20 alkylcarboxylamino, CO2H, cyano, halo, HO; B, B', B'' = H, C1-20 acylamino, C1-20 acyloxy, C1-20 alkanoyl, C1-20 alkenoyl, C1-20 alkoxycarbonyl, C1-20 alkoxy, C1-20 alkylamino, C1-20 alkylcarboxylamino, aroyl, aralkanoyl, CO2H, cyano, halo, HO; or A and B together, or A' and B' together, or A'' and B'' together, may be joined to form a methylenedioxy or ethylenedioxy group; and X, X' are independently -NH, -NR''', O or S]. In contrast to previously reported thiazolidinedione compds., known to lower leptin levels, the present compds. increase leptin levels and have no known liver toxicity. They inhibit the activity of TNF-alpha, interleukin IL-1 or IL-6 or cyclooxygenase-2 (COX-2). The compds. are disclosed as useful for a variety of treatments including the treatment of inflammation, inflammatory and immunol. diseases, insulin resistance, hyperlipidemia, coronary artery disease, cancer and multiple sclerosis. Thus, To a mixture of 3,5-dimethoxybenzaldehyde (500 g) and p-hydroxyphenylacetic acid (457 g) was added acetic anhydride (1 L) and triethylamine (420 mL) and the nonhomogeneous mixture on heating became homogeneous at 70° and stirred at 130-140° for 6 h to give 47% 3-(3,5-dimethoxyphenyl)-2-(4-hydroxyphenyl)acrylic acid (II) (428 g). II (427.5 g) was suspended in 3 L methanol, treated with 100 mL concentrated H2SO4, and heated at reflux for 20 h under Ar to give 97% 3-(3,5-dimethoxyphenyl)-2-(4-hydroxyphenyl)acrylic acid Me ester (III). III (433 g) was dissolved in 1.6 L DMF, treated with 60.4 g NaH (50% in oil) and the with 185 mL p-fluorobenzaldehyde, and heated at 180° for 18 h to give 77% 3-(3,5-dimethoxyphenyl)-2-[4-(4-formylphenoxy)phenyl]acrylic acid Me ester which (352 g), 2,4-thiazolidinedione 98.6, benzoic acid 134, and piperidine 107.4 g were heated in 2.5 L toluene at reflux with continuous removal of H2O through Dean-Stark apparatus to give 86% 3-(3,5-dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylidenemethyl)phenoxy]phenyl]acrylic acid Me ester (IV). IV (30 g) was hydrogenated over 15 g 10% Pd-C in 900 mL dioxane in a Parr apparatus at 60 Psi for 24 h, followed by adding 15 g 10% Pd-C and continuing the hydrogenation for another 24 h to give 86% 3-(3,5-dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenoxy]phenyl]acrylic acid Me ester (V). When V was orally administered to ob/ob mice with a single oral dose (50 mg/kg body weight), there was a 62 % drop in blood glucose level and, similar to db/db mice, there was no significant increase in body weight between the control and the treatment groups. This was in contrast to treatment of diabetic animals by thiazolidinedione type compds. which are known to be associated with increase in body weight

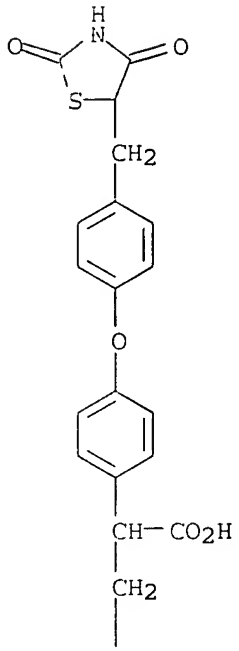
IT 380881-49-2P, 3-(3,5-Dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenoxy]phenyl]propionic acid
380881-51-6P, 3-(3,5-Dimethoxyphenyl)-2-[4-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenoxy]phenyl]propionic acid methyl ester
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel heterocyclic analogs of phenylethylene compds. as inhibitors of cytokines or cyclooxygenase for therapeutic agents)

RN 380881-49-2 CAPLUS

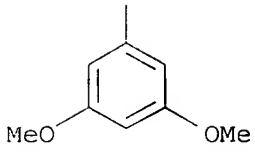
CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy- (9CI) (CA INDEX NAME)

CAS ONLINE PRINTOUT

PAGE 1-A



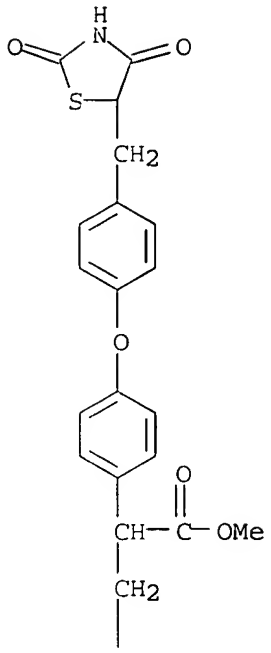
PAGE 2-A



RN 380281-51-6 CAPLUS
CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)

CAS ONLINE PRINTOUT

PAGE 1-A



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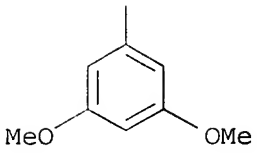

L3 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:923567 CAPLUS
DN 136:37596
TI Preparation and activity of diphenylethylene thiazolidinedione or oxazolidinedione compounds as antidiabetics or antiinflammatories
IN Neogi, Partha; Nag, Bishwajit; Medicherla, Satyanarayana; Dey, Debendranath
PA Calyx Therapeutics, Inc., USA
SO PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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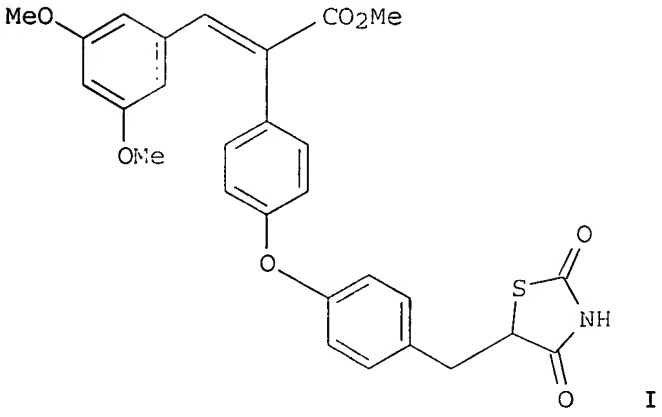


I

AB Novel diphenylethylene compds. and derivs. thereof containing thiazolidinedione or oxazolidinedione moieties are provided which are effective in lowering blood glucose level, serum insulin, triglyceride and free fatty acid levels in animal models of Type II diabetes. In contrast to previously reported thiazolidinedione compds., known to lower leptin levels, the present compds. increase leptin levels and have no known liver toxicity. Thus, (I) was prepared in five steps by condensation of 3,5-dimethoxybenzaldehyde with 4-hydroxyphenylacetic acid followed by esterification and etherification with 4-fluorobenzaldehyde and condensation with 2,4-thiazolidinedione and hydrogenation of the ylidene double bond. Oral administration of I to obese mice caused a 62% drop in blood glucose level. The compds. are disclosed as useful for a variety of treatments including the treatment of inflammation, inflammatory and immunol. diseases, insulin resistance, hyperlipidemia, coronary artery disease, cancer and multiple sclerosis.

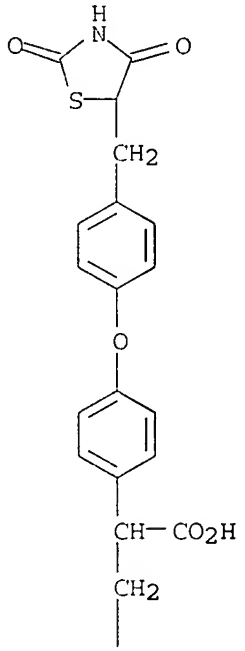
IT 380881-49-2P 380881-51-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation and activity of diphenylethylene thiazolidinedione or oxazolidinedione compds. as antidiabetics or antiinflammatories)

RN 380831-49-2 CAPLUS

CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy- (9CI) (CA INDEX NAME)

PAGE 1-A



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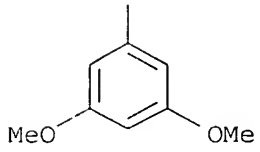
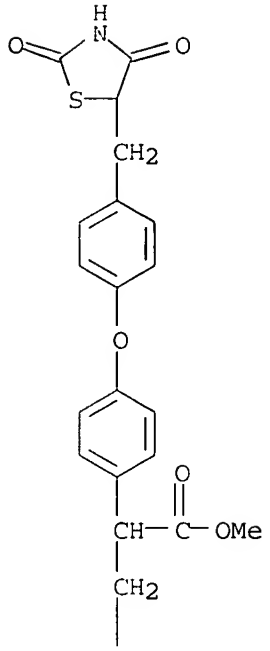


RN 380881-51-6 CAPLUS

CN Benzenepropanoic acid, α-[4-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenoxy]phenyl]-3,5-dimethoxy-, methyl ester (9CI) (CA INDEX NAME)

CAS ONLINE PRINTOUT

PAGE 1-A



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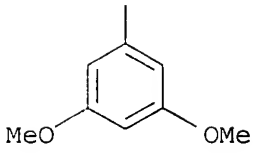

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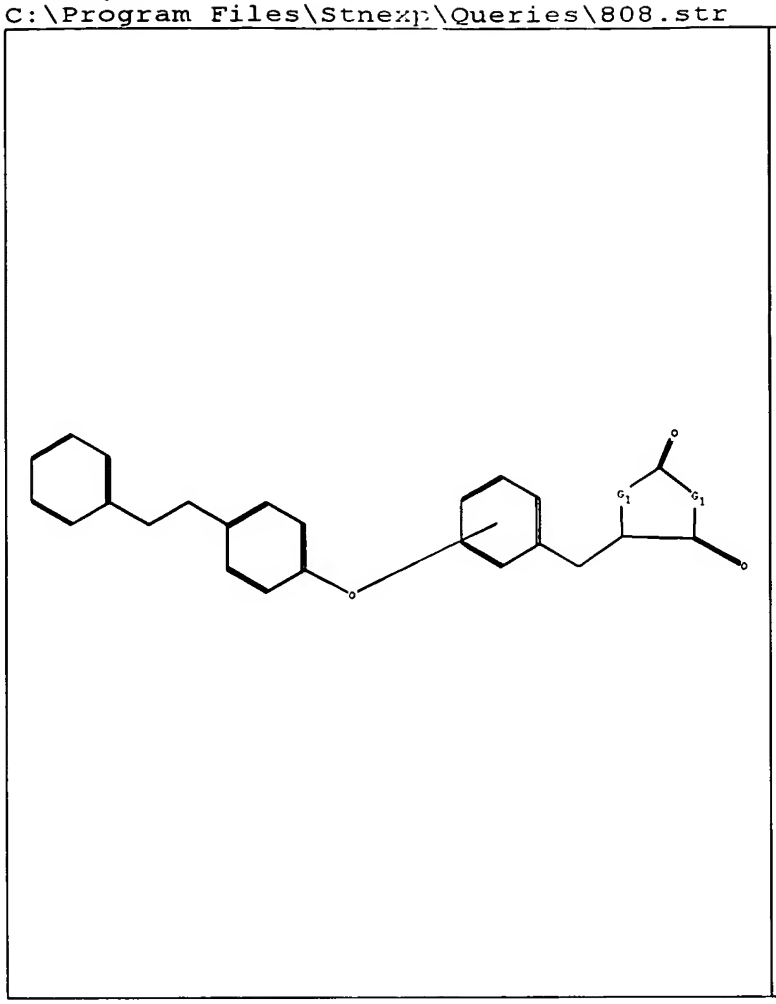

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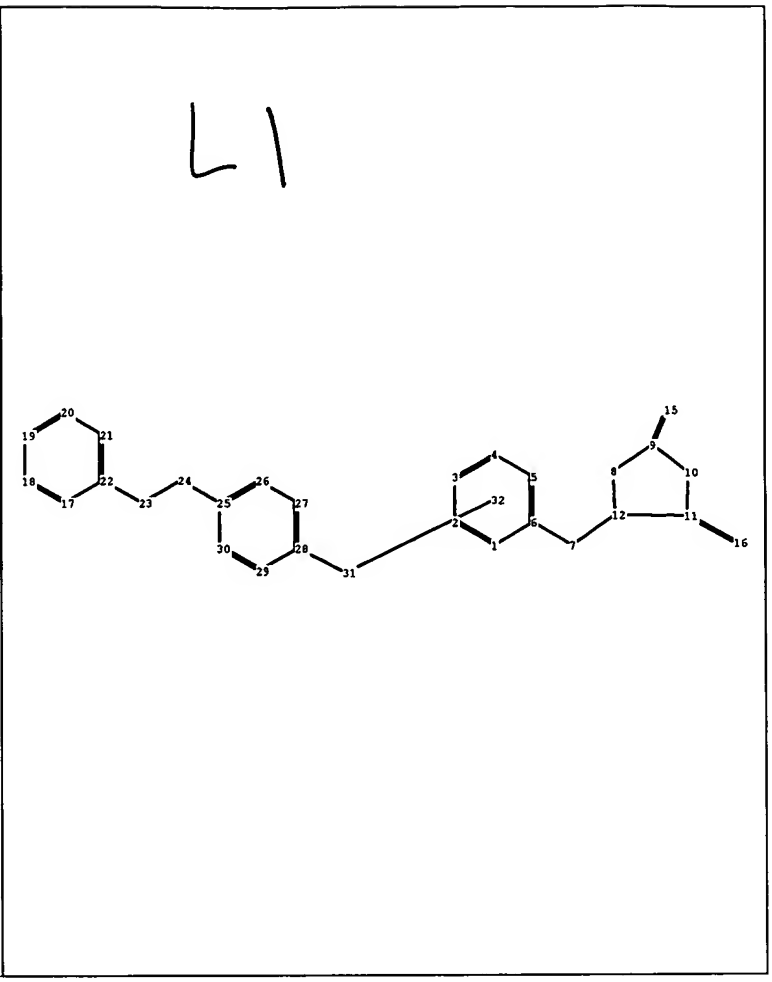

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ring bonds :
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G1:O,S,N

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